

D9 Sub 32  
cont

27. A protein according to claim 11, wherein the protein is a dimmer.--

Add 33

### REMARKS

Claims 6, 9, 11, 13, 16, 20-22 and 24-27 are pending in this application. By this Amendment, claims 2-5, 7, 10, 14-15, 17-18, 20 and 23 are canceled, claims 6, 9, 11, 13, 16, 20-22 and 24-25 are amended and claims 26-27 are added. No new matter is added.

### Claim Numbering

The Office Action indicates that the claims have been renumbered. Apparently no claims 11-12 had been included in this application previously. Applicants have amended the numbering in the pending claims for clarification.

### Claim Rejections - 35 U.S.C. § 101

Claim 22 is rejected as directed to a product of nature and thus is asserted to be non-statutory subject matter. Applicants have amended claim 22 to recite an "isolated" protein, in accordance with the Examiner's suggestion. Reconsideration and withdrawal of the rejection of claim 22 are respectfully requested.

### Claim Rejections - 35 U.S.C. § 112, second paragraph

Claims 6 and 9 continue to be rejected as indefinite for reciting "functional parts thereof" because allegedly it is unclear what "function" or "parts" are intended. While Applicants disagree with the Examiner, in order to expedite prosecution of this application, claim 6 has been amended to define the mature protein alone or in combination with a propeptide or signal peptide. Applicants have also added a new claim 27 defining the proteins as being in dimeric form.

Claims 9, 13 and 24 are again rejected as indefinite for reciting the term "auxiliary". These claims have been amended to no longer contain the term "auxiliary."

Claims 6, 9, 11, 13, 16 and 21 are rejected as indefinite for reciting the term "mature" because the specification allegedly does not disclose that element or combination of elements which is definitive of "mature". Applicants respectfully note that it is mentioned throughout the specification that the nucleic acid sequence coding for the mature protein extends from nucleotides 1782-2142. Claim 11 has been amended to make this even more clear in the claim.

Claims 6, 9, 11, 13, 16 and 23, 24 and 25 are rejected as indefinite for reciting the term "mitogenic activity" because it is allegedly unclear what mitogenic activity is intended. The objectionable terminology has been deleted from the claims.

Claim 11 is objected to apparently because "e)" can be read as being broader than "a), b), and c)." Claim 11 has been amended such that "e)" can no longer be read in such a way.

Claim 20 is objected to for depending from canceled claim 19. Claim 20 has been amended to depend from claim 25.

Claim 21 is objected to because the Examiner apparently does not understand the meaning of "signal peptide or propeptide parts" Claim 21 has been amended to include "signal peptide or propeptide."

Reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, second paragraph, are respectfully requested.

**Claim Rejections - 35 U.S.C. § 112, first paragraph**

Claims 6, 9, 11, 13, 16, 23, 24 and 25 are rejected as not being enabled. The Examiner states in particular that the specification is not being sufficiently enabled by the specification. The Office Action asserts that the specification and claims do not indicate what distinguishing attributes are shared by the members of the genus of mature, active portions of the TGF- $\beta$  family member protein.

However, Applicants respectively note that the specification describes that the protein according to the invention exhibits tissue-inductive biological properties such as osteo-inductive and/or mitogenic capabilities.

Reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph, are respectfully requested.

**Sequence**

The Raw Sequence Listing Error Report indicates informalities in the Sequence Listing filed in this application. Applicants have corrected these informalities in conjunction with the response to the Office Action.

**Conclusion**

Applicants respectfully submit that this application is in condition for allowance and such action is earnestly solicited. If the Examiner believes that anything further is desirable in order to place this application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned representative at the telephone number listed below to schedule a personal or telephone interview to discuss any remaining issues.

Please charge any fee deficiency or credit any overpayment to Deposit Account No. 01-2300.

Respectfully submitted,



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**Pending Claims 6, 9, 11, 13, 16, 21-22 and 24-25 (formerly claims 6, 9, 13, 15, 18, 23-24 and 26-27, respectively) (marked-up to show amendments)**

Cancel claims 2-5, 7, 10, 14-15, 17-18, 20 and 23

6. (Twice Amended) The isolated protein as claimed in claim 11 [13],  
wherein

the protein has the amino acid sequence shown in SEQ ID NO. 2, the mature part thereof or the mature part combined with the propeptide [or functional parts thereof].

9. (Twice Amended) The pharmaceutical composition as claimed in claim 13 [15] wherein the pharmaceutical composition is suitable for the treatment of bone, cartilage or connective tissues or teeth.

11 [13]. (Amended) An isolated protein of the TGF- $\beta$  family encoded by an isolated DNA molecule which comprises a sequence selected from the group consisting of:

- a) the sequence shown in SEQ ID NO:1,
- b) a part of SEQ ID NO:1 which encodes nucleotides 1782-2142 and encodes the mature protein,
- c) a nucleotide sequence which encodes the amino acid sequence according to SEQ ID NO:2,

d) a nucleotide sequence which encodes a portion of the amino acid sequence according to SEQ ID NO:2, wherein said portion is the mature protein, and

e) [the sequence according to a), b), c) or d) which encodes at least a functional part of the protein of the TGF- $\beta$  family, wherein the functional part maintains essentially the same osteo-inductive and/or mitogenic activity of the mature protein, and

f)] a nucleotide sequence which encodes a portion of the amino acid sequence according to SEQ ID NO:2, wherein said portion comprises the seven cysteine region as shown in SEQ ID NO: 13 and which has essentially the same osteoinductive activity of the protein [is the signal or propeptide part].

13 [15]. (Amended) A pharmaceutical composition comprising at least one protein according to claim 11 [6, further comprising a pharmaceutically acceptable carrier, auxiliary substance, diluent or filler].

16 [18]. A dental implant which contains the protein according to claim 11 [13].

20 [22]. A pharmaceutical composition according to claim [19] 25, wherein said matrix material is a biocompatible porous material that can be biologically degraded.

21 [23]. An isolated protein of the TGF- $\beta$  family encoded by a DNA molecule which comprises the part of SEQ ID NO:1 which encodes the mature protein

and further comprises nucleotide sequences coding for at least one of signal peptide or propeptide [parts].

22 [24].     An isolated [A] protein of the TGF- $\beta$  family encoded by a DNA molecule which comprises nucleotides 640-2142 of SEQ ID NO:1.

24 [26].     The pharmaceutical composition as claimed in claim 13 [15], for application in cases where angiogenesis is advantageous or desired.

25 [27].     A pharmaceutical composition comprising at least one protein according to claim 11 [13], wherein the protein is contained on and/or in a natural or synthetically prepared matrix material.

--26.     A pharmaceutical composition according to claim 13 further comprising a pharmaceutically acceptable carrier, diluent or filler.

27.     A protein according to claim 11, wherein the protein is a dimer.--